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(57) Abstract

Agent for treatment and prevention of diarrhoea and gastric ulcers in animals and humans, consisting of a mixture of a pectinaceous plant fibre material with a phospholipid, said agent being obtained by adding to the plant fibre material prior to the admixture of phospholipid under intensive stirring a physiologically acceptable liquid organic substance having a surface tension which is significantly lower than that of water, and method of preparing said agent comprising mixing under intensive stirring the finely-milled, dried pectinaceous plant fibre material with 2 to 10 % by weight of an organic substance based on the plant fibre material, preferably at least one alcohol, and subsequently adding under stirring from 5 to 15 % by weight of lecithin based on the plant fibre material and heated to a temperature of more than 45 °C to obtain a homogeneous mixture.

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PHARMACEUTICAL COMPOSITION CONTAINING PECTIN AND A PHOSPHOLIPID, USED AS AN ANTIDIARRHEAL AND ANTIULCER AGENT

The present invention relates to a novel modified plant fibre preparation with a curative and prophylactic effect on acute infectious diarrhoea and chronic and subchronic, partially symptomless progressing diseases, including infections in the gastrointestinal tract.

Furthermore, the same preparation has surprisingly been found to have a curative effect on gastric ulcers.

Besides, the invention, which is a further development of DK patent No. 153,442 owned by the inventor, implies a substantial simplification of the manufacturing technique compared to that of the above DK patent.

It has long been known that plant fibres in general and in particular fibres having a high content of pectic substances (polygalacturonic acid complexes) exhibit a favourable effect on infectious and non-infectious diarrhoea.

Whereas the use of pectic substances previously rested on a purely empirical basis both within the popular medicine and in a more pharmaceutical-industrial connection, their effects today may be described as effects intervening in some of the pathophysiological mechanisms determining the development of the most widespread types of infectious diarrhoea.

Thus, numerous scientific investigations have demonstrated that the most widespread types of infectious diarrhoea, such as the enterotoxic Escherichia coli diarrhoea, and some virus-related types of diarrhoea are caused by disorders in the enzyme-related mechanisms which via the epithelium of the small intestine maintain a balance prevailing b tween liquid absorption and liquid secretion.

The disorder in the enteral liquid regulation caused by bacteria or virus infection typically results in a drastic reduction in the liquid absorption simultaneously with an excessive increase in the liquid secretion from the intestinal wall out into the bowel contents, which as a result of various self-increasing effects causes the development of diarrhoea.

It is generally known that these basic enzyme-related mechanisms of the diarrhoeic pathogenesis all require a prior adhesion of the pathogenic microorganisms to the outer cell layer of the intestinal epithelium, upon which the adhesion is quickly followed by a heavy bacterial proliferation. The adhesion followed by propagation, referred to as bacterial colonisation, is thus the first step of the diarrhoea-producing mechanisms described above.

As far as the pathogenesis of virus infections is concerned, it may be stated that the dysregulation of the liquid balance and the diarrhoea resulting thereof are caused by a damage of the epithelial cells associated with the virus infection.

Based on the above diarrhoeic pathogenesis, the latest patent literature contains descriptions of diarrhoeic agents which aim at intervening in the initial mechanisms decisive for the development of diarrhoea, the attention being particularly paid to the importance of hydrophobic/hydrophobic bonds, the so-called "like-like" interactions", e.g. for the development of Escherichia coli infections.

In order to intervene in some of the forces applying to the bacterial colonisation, EP patent publication No. 0 021 230 describes an agent comprising one or more polymeric carbohydrates or sugars having a hydrophobic group and a molecular weight which is sufficiently high to prevent them from penetrating a cellular membrane, and a physiologically acceptable inorganic material having a hydrophobic surface layer.

The purpose of using said combination of a polymer having a hydrophobic group and an inorganic material having a hydrophobic surface layer is to attract the pathogenic bact ria and to cause these to adhere to the polymer and the inorganic material rather than to the cell tissue, e.g. the intestinal cell tissue. The prior art agent does not contain pectin and the introduction of the hydrophobic group on the polymer is based on a chemical reaction, viz. an etherification, esterification or amidation.

DK patent No. 153 442 B belonging to the Applicant describes an agent based on a pectinaceous material for the treatment and prevention of diarrhoea in humans and animals, which agent is characterized in further comprising an amphophilic substance containing a long-chained hydrophobic group for increasing the effect of the pectinaceous material. The agent is characterized in that the amphophilic substance is lecithin.

Both patents mentioned maintain that the effect is attributable to an active intervention in the hydrophobic bonds between hydrophobic bacterial capsule antigens (adhesins, hydrophobins) and corresponding hydrophobic structures in the cell walls of the intestinal epithelium which are considered to be of decisive importance for the development of the bacterial colonisation.

However, continued investigations have shown that other points of views may be adopted as to said mechanism of action, and that the product described in DK patent No. 153,442 B may be further improved, as said product, even though its curative and prophylactic effect on infectious diarhoea have been demonstrated through treatment of several million calves, suffer from certain drawbacks, among which the following should be emphasized:

- The effect on acute infectious diarrhoea in pigs is not satisfactory.
- Aqu ous suspensions of the agent are not sufficiently stable.

Both drawbacks are remedied with the present invention which consists of an agent for treatment of diarrhoea and gastric ulcers in animals and humans, said agent comprising a mixture of a pectinaceous plant fibre material with a phospholipid, characterized in that said agent is obtained by adding to the plant fibre material prior to the admixture of phospholipid under intensive stirring a physiologically acceptable liquid organic substance having a surface tension significantly lower than that of water. The agent according to the invention simultaneously provides a clinical effect also in case of symptomless progressing intestinal infections of a subchronic type, such as e.g. in case of Salmonella disease carrier states among poultry and pigs.

For both of the mentioned categories of intestinal infections it strongly applies that the affections associated with the bacterial colonisation are found not only in the anterior sections of the small intestine but also in the posterior sections thereof and in the colon.

This implies that an agent directed towards combatting these infections should possess a colloidal stability and activity which are sufficiently high to maintain the interfering effect of the colonisation for a maximum extent through the intestinal tract.

Moreover, it is of decisive importance that after suspension in the aqueous phase of the bowel contents the agent is quickly combined with said phase under the simultaneous formation of a gel.

Laboratory tests and clinical investigations hav shown that surprisingly said problems can be remedied with th particular m thod of the present inv ntion, which method consists in that prior to the mechanical mixture with lecithin the pectic fibres are conditioned with a physiologically acceptable organic liquid which contributes to increase the interface potential toward the aqueous phase and simultaneously makes the fibres more available to the lecithin.

Said liquid is preferably selected among alcohols, such as ethanol, glycerol, propylene glycol, polypropylene glycol, polyethylene glycol and mixtures thereof.

It has been found that a non-toxic monohydric alcohol, ethanol, a trihydric alcohol, glycerol or mixtures of these are particularly suitable as a physiologically acceptable, liquid organic substance having a surface tension lower than that of water.

It is preferred that the alcohol used is not removed again, but that it forms an integrated component of the finished product.

Besides, pyrrolidone-containing compounds, incl. polyvinyl pyrrolidone (PVP), may be used as a physiologically acceptable liquid organic substance. Polyvinyl pyrrolidone may be used in an aqueous solution at a concentration of 3-5% (w/w).

The organic substance may also be ethoxylated sorbitan fatty acid esters, which compounds are also known as polysorbates and Tween compounds. The ethoxy moiety of the compounds may be the polyoxy ethylene, and the fatty acid moiety may be C_3-C_{18} fatty acids and derivatives thereof, preferably lauric acid, palmitic acid, stearic acid, and oleic acid.

The ethoxylated sorbitan fatty acid esters may be used alone or in combination with cellulose or a derivative thereof, such as methyl cellulose.

Finally, the organic substance may be comprised of a mixture of two or more of the above mentioned substances. A mixture of an alcohol and an ethoxylated sorbitan fatty acid ester is preferred due to their mutually promoting effects.

The organic substance may be used together with a promoter which enhances the above mentioned effect. Examples of such a promoter are mono- or diesters of propylene glycol and edible fatty acids.

A preferred embodiment of the invention uses a pectinaceous plant fibre material selected among potato pulp, citrus residues, apple residues, soya bean fibres, and similar materials constituting from 65 to 90% by weight of the finished mixture, and the alcohol used is ethanol or a mixture of ethanol and glycerol constituting from 2 to 10% by weight of the finished mixture based on the plant fibre material, and the phospholipid is any physiologically acceptable lecithin constituting from 5 to 15% by weight of the finished mixture.

Furthermore, the invention relates to the use of the agent defined in claims 1-4 for treating disorders associated with the alimentary tract in animals and humans, in particular disorders caused by Salmonella infection in the intestinal tract in mammals and birds, preferably chickens, pigs and calves, and gastric ulcers in mammals, in particular belonging to the unguinae order, and humans.

Finally, the invention relates to a feedstuff, preferably containing from 2 to 10% by weight of the agent according to the invention. A typical chicken feedstuff composition is 19% by weight of soya meal, 15% by weight of rapeseed, 33% by

weight of wheat, 21% by weight of peas, 4.6% by weight of meat-and-bone meal, 2.6% by weight of fat, 1.8% by weight of minerals and vitamins, and 3.0% by weight of th agent according to the invention.

In order to obtain a partial simulation of the effect of diffently made preparations with regard to dispersion through the bowel content and of the effect with regard to physical influence on the consistency of the bowel content, comparative rheological tests have been made, in which the effects of the agent of the invention composed according to example 1 below were compared with the effects of a corresponding, non-alcohol-enriched fibre product consisting of:

dried potato pulp	158 g
citrus residues	50 g
silicium dioxide	2 g
lecithin	40 g
	250 g

Comparative rheological tests surprisingly show that a significant improvement of the effect of the pectin-lecithin mixture on the consistency of the bowel content is obtained with the agent according to the invention.

Thus, the effect obtained with the improvement is that the conditioning of the pectic fibres with an alcohol mixture effected in accordance with the invention causes the fibres to combine momentarily with the bowel content under the formation of a homogeneous, gelatinaceous phase. After 8 hours this phase was found to be stable and showed no syneresis (liberation of water).

A similar rheological effect could not be obtained by mixing the bowel content with the corresponding non-alcohol-treated pectic fibre pr paration, as said preparation showing no

gelatinac ous properties would only be allowed to be combined with the bow l content under intensive mechanical influence.

The observed rheological effect, which is of a surprising nature, is important also in therapeutic connections, as it reflects a desired colloidal-chemical modification of the micro-structures to which adhesive potentials in respect of colonized bacteria cells may be attributed ipso facto.

Furthermore, continued comparative tests have shown that the preparation conditioned with alcohol is much more suspendable than the non-conditioned preparation.

Whereas the analogous, non-pretreated pectin-phospholipid mixture after stirring into water is quickly precipitated as a coherent mass, the alcohol conditioned product is kept floating in the liquid as an evenly distributed phase of agglomerated, macroscopically visible particles.

The invention will now be further illustrated by a number of examples.

EXAMPLE 1

A mixture is prepared of:

dried potato pulp		150 g
citrus residues		50 g
ethanol 99% v/v	5 g	10 g
glycerol	5 g	
lecithin		40 g
		250 g

After mechanical mixing of the two fibre products, potato pulp and citrus residues, the two mixed alcohols are added to the mixture. In this connection it is noted that the volume of the fibres is reduced. Lecithin heated to 45°C is add d

after intensive mechanical stirring. Effective mixing of lecithin with the alcohol conditioned fibres is then obtained within a few minutes by continued mechanical stirring.

EXAMPLE 1.-B

Milled, dried citrus residues (A/S Københavns Pektinfabrik - having a water content of 12% and an average particle size of 0.5 mm) are mixed under intensive mechanical stirring with 4% by weight of an equal mixture of ethanol (99%/surface tension: 22.3 mN/m) and glycerol.

After completion of the mixing, which is characterized by a reduction of the volume of the fibre substance by about 15%, the method for condensation with lecithin defined in DK patent No. 153,442 B is carried out.

The product made, Mixture A, is compared by carrying out comparative Langmuir-Adam measurements and H.I.C. tests with a non-alcohol-enriched but otherwise identical pectin-lecithin mixture, Mixture B, to which a granulation agent is added (technical additive).

In carrying out these tests a Langmuir-Adam surface balance apparatus is used which registers the changes in the surface tension of water after application of the preparation on the surface of the water in terms of the measuring unit mN/m.

Similarly the bacterial cell adsorbing effect of each preparation was measured and registered by carrying out H.I.C. tests (Hydrophobic Interaction Chromatography).

Langmuir-Adam Surface Balance Methodology

The application of an insoluble, non-volatile organic substance to the surface of water having a relatively high surface tension (τo = 72,8 mN/m) results in either:

1: The formation of a compact drop leaving the remaining water surface pure, or

2: The formation of a monolayer film which is dispersed over the entire water surface due to the interactions between water and the substance concerned.

In other words, the formation and maintenance of a monolayer depend on the adhesive forces between water and the constituent molecules of the monolayer being stronger than the cohesive forces applying to the substance.

The formation of monolayers and the determining forces thereof are identical, irrespective of whether free water surfaces, i.e. water/gas surfaces, or interfaces between water and other separated phases, such as solid substances, oil or gel phases, are concerned.

The reduction of the interface tension exerted by the monolayer corresponds to the surface pressure of the monolayer: Π. The expanding pressure thereby produced thus counteracts the contracting tension of the pure water surface, which will always be very distinct due to the intimate bonds of the H-bridges.

$\Pi = \tau o - \tau$

τo = the tension of the pure surface.

τ = the tension relating to the interface monolayer.

According to Gibb's theory, changes in the surface tension of water, $\Delta\tau$, and the maintenance of this effect in time will

thus reflect the adsorptive capacity and stability of the monolayer.

In the Langmuir-Adam apparatus the surface pressure exerted by the monolayer is determined directly by measurement of the horizontally acting force by which the monolayer affects a floating body placed in the monolayer/water interface, see "Lipid and Biopolymer Monolayers at Liquid Interfaces", Birdi K.S., p. 292, Plenum Press, New York, 1989.

H.I.C.-Tests
Hydrophobic Interaction Chromatography
Measurement of bacteria cell adsorbing capacity

In the H.I.C. test the capability of various pectin-lecithin preparations to bind strains of diarrhoea-producing bacteria is determined by eluation of a pectin-lecithin impregnated Octyl-Sepharose column with a suspension of bacteria cells in a predetermined concentration.

Following column eluation the eluate is subjected to a spectophotometric measurement in order thereby to determine the amount of bacteria cells retained on the column (% cells adsorbed).

Mixture A		Mixture B	
Citrus residues	50 g	Citrus residues	50 g
Ethanol/glycerol aa. p.	2 g	Lecithin	18 g
Lecithin	18 g	Silicium dioxide*	2 g
	70 g		70 g

* Granulation agent

The results of the measurements effected are shown in Table 1.

	Mixture A.	Mixture B.
Langmuir-Adam (mN/m).	43 mN/m	8 mN/m
H. I .C. (% E. coli-cells adsorbed).	96%	54%

The measuring results shown in Example 1-A state the average of double determinations.

Supplementary investigations of 10 diffently made preparations, carried out as concurrent Langmuir-Adam measurements and H.I.C. tests, all showed a clear congruity between mN/m-values (maximum interface potential) and H.I.C. results (maximum % of E. coli cells adsorbed to the column).

Thus, the tests indicate that the bacteria eliminating effects primarily may be attributed to the colloidal-chemical relating interface potentials.

EXAMPLE 2

In a clinical test with diarrhoeic pigs the curative effect of an agent prepared according to the present invention is compared with the effect of a corresponding agent, prepared without preconditioning of the pectic fibre substance with alcohol.

The test was carried out on a large specific-pathogen-free pig herd, wher all diarrhoeic pigs are isolated in a separate section of th climatic housing section designed for weaning piglets, which provides the possibility of carrying out comparative treatment tests on a uniform animal herd.

According to microbiological investigations the diarrhoeic pigs can be characterized by infection with E.coli 0149 K88, i.e. an Escherichia coli strain having antigen 0149 which is characteristic of pig pathogenicity and adhesin K88 which is responsible for adhesive properties (pig specific capsule antigen). This strain is sensitive to colistin-sulphate but resistant to most other antibiotics.

A total of 38 pigs are put in the isolated housing section. Criteria for admission: diarrhoea accompanied by poor growth.

The 38 diarrhoeic pigs are divided into 4 groups, to which 4 small housing sections are allocated with 9-10 pigs in each.

Groups 1 and 3 (18 pigs) are treated with the pectic fibre phospholipid preparation prepared according to the present patent application.

Groups 2 and 4 (20 pigs) are treated with a pectic fibre phospholipid preparation which is identical with the one used for groups 1 and 3 except that the pectic substance used therein is not pretreated with an ethanol-glycerol mixture, compare the composition of the two test preparations, Table 2.

TABLE 2

Component	Test preparations for the treatment of: Groups 1 + 3	Groups 2 + 4
Citrus residues	222.0 g	227.0 g
Potato pectin	119.0 g	124.0 g
Ethanol	5.0 g	-
Glycerol	5.0 g	-
Lecithin	136.5 g	136.5 g
Electrolyte glucose*	512.5 g	512.5 g
	1,000.0 g	1,000.0 g

*) Electrolyte-glucose mixture for momentary rehydration of diarrhoeic pigs, composed of:

NaCl, $NaHCO_3$, KCl, citrate and glucose.

Table 2 Composition of test preparations with and without preconditioning with ethanol-glycerol mixture and application of said compositions for 4 test groups.

Both test preparations are stirred into water at 35 g per liter of water given to each group as drinking water ad libitum.

The pigs are checked 3 times daily, the number of pigs suffering from diarrhoea and the number showing reduced appetite being recorded each time.

The test is continued for 48 hours after which the treatment is discontinued.

The results of the comparative test of the two preparations are shown in Table 3.

Table 3

Group No. Number of pigs	Number of pigs suffering from diarrhoea after number of hours: 0	8	24	32	48
1 + 3 (18)	18	16	8	6	2
2 + 4 (20)	20	20	16	15	12

As will appear from Table 3, the number of diarrhoeic pigs in Groups 1 and 3 are reduced to 8 after 24 hours. After 48 hours 16 pigs (88%) out of the pigs treated with a product prepared according to the present invention are cured of diarrhoea.

In groups 2 and 4, 16 out of 20 pigs are still suffering from diarrhoea after 24 hours. After 48 hours 8 pigs (40%) out of the pigs treated with a product prepared without preconditioning the pectic fibres, are cured.

EXAMPLE 3

For the treatment of Salmonella-infected chickens the following mixture is prepared:

Dried potato pulp	300 g
Ethanol	30 g
Lecithin	90 g
	420 g

Out of a Salmonella typhimurium-infected flock, 10 chickens are selected. After detection of S. typhimurium by bacteriological investigation of individual dropping samples, the chickens are put in the same house, as they are divided into two separate groups A and B.

Group A is fed with a standard broiler fe dstuff, "Brun Rapsi", K.F.K., 23% crude protein.

Group B is fed with the same feed mixture, admix d with 3% of the above pectin-ethanol-lecithin preparation.

After 9 days all the chickens are killed and subjected to a bacteriological investigation.

The bacteriological investigation shows that the chickens of Group A are still infected with S. typhimurium.

Salmonella are not detected in the chickens of Group B.

EXAMPLE 4

For treatment of gastrointestinal disorders in horses the following mixture is prepared:

Dried potato pulp		1,000 g
Potato pectic fibres ("Potex")		500 g
Citrus residues		1,000 g
Ethanol	75 g	
		150 g
Glycerol	75 g	
Lecithin		600 g
Dried potato pulp		1,000 g
Apple residues		400 g
		4,650 g

As exemplified below the preparation is used as a curative agent in single doses of 300 g against diarrhoea and ulcer diseases in full-grown horses.

Diarrhoeic states
4-year-old trotting stallion

Through half a year the stallion has suffered from a recurring diarrhoea with foul stool. He is very nervous and his performances on the track are poor. The stallion has repeatedly been treated with preparations of Lactobacillus and different antibacterial agents prescribed by the veterinary but there has been no improvement of his condition.

The treatment with the agent according to the present invention is carried out twice at an interval of 10 days.

In each treatment 3 x 300 g are administered the first day followed by 300 g daily for 7 days. After the first treatment the diarrhoea had stopped, and the condition of the horse had significantly improved. When the horse again had mild outbreaks of diarrhoea and showed nervous symptoms on the track, the same treatment was repeated 10 days later. After two months there has been no recurrence of diarrhoea and the performance of the horse is now very satisfactory.

7-year-old riding horse

The horse, which is regularly used in competitions, has suffered from foul diarrhoea and at the same time extreme nervousness through several months. It has been treated repeatedly with preparations of Lactobacillus, various obstipantia and other agents prescribed by the veterinary without any change in the condition.

A treatment with the present agent, prescribed by the general veterinary, and administered at 3 x 300 g the first day followed by 300 g daily for 8 days, caused a permanent disappearance of all symptoms. The horse has been symptom-free for 3 months.

Gastric ulcers

According to rec nt inv stigations in this country and abroad gastric ulcers are a frequently occuring disease in trotting horses and other horses which are used regularly in competitions.

Symptoms of the disease are typically:

The appetite of the horse is noticeably reduced, it eats the feedstuff in small portions, as it exhibits signs of a mild colic after each short feedstuff intake, it then returns to the trough, eats a small portion, becomes uneasy, etc. Without being really emaciated the horse is thin with taut belly, mat pelt layer and lack-lustre, sunken eyes. The horse is nervous, stressed and its performances on the track are extremely poor.

"Sleipner" a 5-year-old trotting stallion

The stallion, which initially had been sold for slaughtering due to his poor performances, is purchased for DKK 5,000 and stabled at a stud farm in Northern Jutland.

Symptomatic of ulcer diseases the stallion exhibits: mild attacks of colic in connection with each feedstuff intake, he eats the feedstuff in small portions with many intermissions. The horse is lean having a mat pelt layer. His performances are extremely poor: trots 800 m at a maximum.

After 10 days of treatment with the agent according to the invention the stallion is symptom-free; he eats normally and shows no signs of colic or the stress associated therewith.

After 2 months' training the stallion is chosen to participate in Dansk Travderby where he is proclaimed favorit

candidate to win after having won the pr liminary race. Owing to a virus-r lat d tonsillitis attack 2 days before the race he ends up as No. 4 in the 1994 Derby race. Subs quently the horse wins several races in the summer of 1994.

There is a total of 29 registered treatments of similar cases with trotting horses. All treatments carried out by general veterinaries or by professional trainers resulted in a complete cure, irrespective of whether actual diarrhoea or as in most cases ulcer diseases were involved.

Treatment of calves

26 calves having symptoms of gastric ulcers were treated with the preparation described above. Positive treatment results were registered in all cases.

EXAMPLE 5

Two recently acquired calves, about 8 weeks old, which are admitted into a particular fattening calf herd exhibit characteristic symptoms of gastric ulcers 1 week after the admission.

Both calves are emaciated. They are feeble and their urge to drink and eat is strongly reduced. The calves are non-febrile; there are no symptoms of pulmonary diseases and they do not suffer from diarrhoea.

Auscultation shows that the bowel activity is impaired. Both calves are distended in the right flank in which clear plashing sounds can be detected by deep palpation.

The calves are treated with a preparation consisting of:

Dri d potato pulp	1,000 g
Potato p ctic fibres ("Potex")	500 g
Citrus r sidu s	1,000 g
Aqueous solution of polyvinyl pyrrolidone ("Polyvidon DLS 86") 5% (w/w)	200 g
Lecithin	600 g
Dried potato pulp	1,000 g
Apple residues	400 g
	4,700 g

The agent is administered at a dosage of 2 x 50 g per day for 3 days followed by 1 x 50 g per day for 8 days.

After 2 days the distention of the right flank is reduced, the calves begin to drink milk replacer, the appetite is increased, and the condition gradually returns to normal within the next week.

Gastric ulcers are a typical chronic disease; it is therefore important that the treatment is continued throughout the entire period in order to prevent relapses.

EXAMPLE 6

Three calves of the same particular slaughter calf herd and having the same symptoms of gastric ulcers as those mentioned in example 5, are treated with a preparation composed of:

Dried potato pulp	1,000 g
Potato pectic fibres ("Potex")	500 g
Citrus residues	1,000 g
Aqueous solution of "Methyl cellulose M 20" 0.5% (w/w) and "Tw en 60" 1.0% (w/w)	120 g
Lecithin	600 g
Dried potato pulp	1,000 g

Apple residues	400 g
	4,620 g

The treatment which is instituted at 2 x 50 g per day for 3 days followed by 1 x 50 g per day for 8 days resulted in full restitution.

PATENT CLAIMS

1. Agent for treatment of diarrhoea and gastric ulcers in animals and humans consisting of a mixture of a p ctinaceous plant fibre material with a phospholipid, characterized in that said agent is obtained by adding to the plant fibre material prior to the admixture of phospholipid under intensive stirring a physiologically acceptable liquid organic substance having a surface tension significantly lower than that of water.

2. Agent according to claim 1, characterized in that the organic substance used is an alcohol or a mixture of alcohols which are not removed after admixture but form a component of the finished agent.

3. Agent according to claim 1, characterized in that the organic substance is a pyrrolidone-containing compound.

4. Agent according to claim 3, characterized in that the organic substance is polyvinyl pyrrolidone (PVP).

5. Agent according to claim 1, characterized in that the organic substance is an ethoxylated sorbitane fatty acid ester.

6. Agent according to any of the preceding claims, characterized in that the pectinaceous plant fibre material is selected among potato pulp, citrus residues, apple residues, soya bean fibres and constitutes from 65 to 90% by weight of the finished mixture, the alcohol used is ethanol or a mixture of ethanol and glycerol constituting from 2 to 10% by weight of the finished mixture based on the plant fibre material, and the phospholipid is lecithin

constituting from 5 to 15% by weight of the finished mixtur based on th plant fibre material.

7. Use of the agent according to claims 1-6 for the treatment of diseases associated with the digestive tract in animals and humans.

8. Use according to claim 7, c h a r a c t e r i z e d in that the disease is caused by Salmonella infection in the intestinal tract in mammals and birds, preferably chickens, pigs and calves.

9. Use according to claim 7, c h a r a c t e r i z e d in that the disease is gastric ulcer in mammals, including humans.

10. Feedstuff for the prevention of diseases associated with the digestive tract, preferably diarrhoea and gastric ulcers, in animals, c h a r a c t e r i z e d in containing an effective amount of the agent according to claims 1-6.

11. Feedstuff according to claim 10, c h a r a c t e - r i z e d in containing from 2 to 10% by weight of the agent according to claims 1-6.

12. Method of preparing the agent according to claims 1-6, c h a r a c t e r i z e d in that the finely-milled, dried pectinaceous plant fibre material is mixed under intensive stirring with 2 to 10% by weight of an organic substance based on the plant fibre material, preferably at least one alcohol, whereafter from 5 to 15% by weight of lecithin based on the plant fibre material and heated to a temperature of more than 45° C is added under stirring to obtain a homogeneous mixture.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 96/00168

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: A61K 45/06, A61K 31/725, A23K 1/14, A61K 35/78
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: A61K, A23K, C09J, C08B, B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPAT, USPM, IFIPAT, USPATFULL, MEDLINE, EMBASE, WPID'S

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	EP 0092121 A1 (THE UNIVERSITY OF TEXAS SYSTEM BOARD OF REGENTS), 26 October 1983 (26.10.83) --	1-12
A	US 4162306 A (H-G LAVES), 24 July 1979 (24.07.79) --	1-12
A	US 5462742 A (C. BOGENTOFT ET AL), 31 October 1995 (31.10.95) -- --------	1-12

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 July 1996	16 -07- 1996
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Carolina Gómez Lagerlöf Teleph ne No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

Information on patent family members

01/04/96

International application No.
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